

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning on page 19, beginning at line 20 with the following:

Results show that collagen similar to that described herein has been observed to remain in the knee joints in animals for up to 8 weeks. Fibrillar, highly purified Type I collagen has previously been shown to be safe for *in vivo* use (Pavelka et al. (June 1999) Poster No. 001096 *XIV European League Against Rheumatism Congress*, Glasgow, Scotland and (June 1999) *4th Congress of the European Federation of National Associations of Orthopaedics and Traumatology*, Brussels, Belgium; Pavelka et al. (September 1999) *Fourth World Congress of the OsteoArthritis Research Society International*, Vienna, Austria). Zyderm[®] ZYDERM, a formulation of insoluble non-crosslinked fibrillar atelopeptide collagen Type I and 0.3% (3 mg/mL) lidocaine is commercially available (Inamed Anesthetics ~~McGhan Medical Corporation~~, Santa Barbara, CA) and used primarily for collagen replacement under the skin. As described in Pavelka (*supra*), 1 mL intra-articular injections of formulations of collagen have been used in the treatment of osteoarthritis. However, results show that the amount of lidocaine present in these injections is not effective for pain management over time, with the anesthetic effects of lidocaine lasting less than an hour, in most cases only a few minutes (*e.g.* less than 10 minutes). Collagen has also been used in a matrix for the controlled delivery of protein growth factors (Shroeder-Teft et al. (1997) *Controlled Release* 49:291-298; Bentz et al. (1998) *J. Biomed. Mater. Res.* 39:539-548; McPherson et al. (1988) *Coll. Relat. Res.* 8(1):65-828:65-82; Rosenblatt et al. (1989) *J. Controlled Release* 9:195-203).

Please replace the paragraph beginning on page 23, beginning at line 6 with the following:

As will also be appreciated by one of skill in the art, the formulation of the composition will also be tailored for the particular pharmaceutical agent which is being delivered, taking into account the effective amount of pharmaceutical agent to be released such that the amount released at a given time, or throughout the duration of delivery, is not toxic to the patient. Information regarding the toxicity and half-life of known pharmaceutical agents is readily available. For example, bupivacaine is known to have a half life in adults of approximately 3.5 hours. A similar compound (levobupivacaine) has been shown to be non-genotoxic by standard mutagenicity and clastogenicity assays (Summary of Product Characteristics for ~~Chirocaine®~~ CHIROCAINE, levobupivacaine for injection). Therapeutic apparently safe doses of bupivacaine are approximately 225 mg as a single bolus. The maximum dose of bupivacaine is 400 mg over a 24 hour period, and a single dose of 4.4 mg/kg (\approx 350 mg in an adult human) produced seizures in research monkeys, while the intravenous and subcutaneous LD₅₀ in mice is 6 to 8 mg/kg and 38 to 54 mg/kg respectively (Physicians Desk Reference, Medical Economic Company, Montvale NJ, 53rd edition).